

line screening;

Fig. 3 shows the results of all L-esters tested on Colo205 cells (colonic cancer); and

Fig. 4 shows the results of all L-esters tested on BxPC3 cells (pancreatic cancer). --

On page 7, between lines 10 and 11, please insert:

-- DESCRIPTION OF VARIOUS AND PREFERRED EMBODIMENTS OF THE
INVENTION –

On page 77, please delete line 1 and insert therefore:

-- WHAT IS CLAIMED IS: --

Amendments to the Claims:

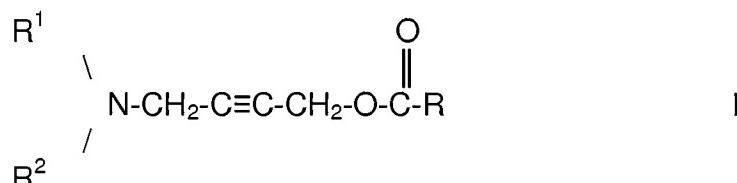
Please amend claims 1 to 12 and add claim 13 as set forth hereinafter.

Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims

1. (Currently Amended) 4-(N-substituted amino)-2-butynyl-1-esters represented by the following general formula I, their bis-(2-butynyl)diesters and pharmaceutically acceptable salts thereof,



wherein

R is a hydrogen atom; a straight-chained or branched, saturated or unsaturated aliphatic radical with 1-20 C-atoms which is unsubstituted or substituted one or more times by C₁-C₆-alkyl, C₁-C₆-alkoxy, halogen, epoxy, amino, mercapto, a phenyl ring which is unsubstituted or substituted one or more times by C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy, epoxy, amino, mercapto or halogen; a cycloalkyl group with 4 to 7 atoms unsubstituted or substituted

one or more times by C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy, epoxy, amino, mercapto or halogen,

R¹ and R² are joined to form a heterocyclic ring with 3 to 6 C-atoms, unsubstituted or substituted one or more times by C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy, halogen, epoxy, amino, mercapto, whereby at least one C-atom can be replaced by O, S or N,

or

R¹ and R² are the same or different a hydrogen atom, a straight-chained or branched, saturated or unsaturated aliphatic radical with 1-20 C-atoms, unsubstituted or substituted one or more times by C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy, halogen, epoxy, amino, or mercapto.

2. (Previously Presented) 4-(N-substituted amino)-2-butynyl-1-esters according to claim 1,

wherein

R is a hydrogen atom, a straight-chained or branched alkyl group with 1-12 C-atoms, which can be substituted one or more times by C₁-C₆-alkyl; a phenyl ring which can be substituted one or more times by C₁-C₆-alkyl; a cyclo alkyl ring with 5-6 C-atoms which can be substituted one or more times by C₁-C₆-alkyl.

3. (Currently Amended) 4-(N-substituted amino)-2-butynyl-1-esters according to claim 1 or 2,

wherein

R¹ and R² are the same alkyl group with 1-12 C-atoms, which can be straight-chained or branched and substituted by C₁-C₆-alkyl,

or

R¹ and R² are joined to form a heterocyclic ring with 4 to 6 C-atoms, whereby at

least one C-atom can be replaced by O, S or N, and the ring can be substituted by C₁-C₆-alkyl.

4. (Currently Amended) 4-(N-substituted amino)-2-butynyl-1-esters according to ~~one of claims 1 to 3~~ claim 1,

wherein

R is a hydrogen atom, a straight-chained or branched alkyl group with 1-6 C-atoms, which can be substituted one or more times by C₁-C₆-alkyl; a phenyl ring which can be substituted one or more times by C₁-C₆-alkyl; a cyclo alkyl ring with 5-6 C-atoms which can be substituted one or more times by C₁-C₆-alkyl,

and

R¹ and R² are the same alkyl group with 1-6 C-atoms, which can be straight-chained or branched and substituted by C₁-C₆-alkyl,

or

R¹ and R² are joined to form a heterocyclic ring with 4 to 6 C-atoms, whereby at least one C-atom can be replaced by O, S or N, and the ring can be substituted by C₁-C₆-alkyl.

5. (Currently Amended) 4-(N-substituted amino)-2-butynyl-1-esters according to claims 4,

wherein

R is H or alkyl such as methyl, ethyl, propyl, butyl, pentyl, hexyl, phenyl, tertiary butyl and cyclohexyl

and

R¹ and R² are identically methyl, ethyl, propyl, butyl or phenyl; or form together with the N-atom a piperidino, pyrrolidino, morpholino, thiomorpholino, hexamethylene imino, piperazino and methyl piperazino ring.

6. (Currently Amended) 4-(N-substituted amino)-2-butynyl-1-esters according to claims claim 5,

wherein 4-(N-substituted amino)-2-butynyl-1-esters are selected from the group comprising

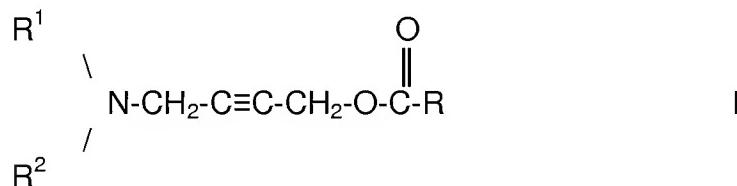
- [N-(4-morpholino-2-butynyl)] acetate
- [N-(4-piperidino-2-butynyl)] acetate
- [N-(4-(N-methyl piperazino-2-butynyl)] acetate
- [N-(4-thiomorpholino-2-butynyl)] acetate
- [N-(4-pyrrolidino-2-butynyl)] acetate
- [N-(4-hexamethylene imino-2-butynyl)] acetate
- [N-(4-morpholino-2-butynyl)] benzoate
- [N-(4-morpholino-2-butynyl)] formate
- [N-(4-diethylamino-2-butynyl)] acetate
- [N-(4-diphenylamino-2-butynyl)] acetate
- [N-(4-morpholino-2-butynyl)] propionate
- [N-(4-thiomorpholino-2-butynyl)] propionate
- [N-(4-morpholino-2-butynyl)] pivalate
- [N,N'-(4,4-piperazino-bis-2-butynyl)] diacetate and
- [N-(4-morpholino-2-butynyl)] cyclohexyl carboxylate.

7. (Currently Amended) Method for producing 4-(N-substituted amino)-2-butynyl-1-esters or a pharmaceutically acceptable salt according to ~~anyone of claims 1-6~~ claim 1 comprising

- a successive conversion of a propargyl alcohol in a propargyl ester by simple esterification,
- a conversion of the propargyl ester in N-(4-amino-2-butynyl) ester by Mannich condensation to give a compound of formula I and, if desired optionally,

converting a compound of formula I to a corresponding pharmaceutically pharmaceutical salt by conventional means.

8. (Currently Amended) Method according to claim 7,
~~characterized in that,~~
wherein the Mannich condensation is performed in the presence of paraformaldehyd, an acid catalyst, Cu-salts and a solvent.
9. (Currently Amended) Pharmaceutical composition for use in therapy, comprising a compound according to ~~anyone of claims 1 to 6~~ claim 1, and a pharmaceutically-acceptable carriers, adjuvants, vehicles and/or diluents carrier, adjuvant, vehicle and/or diluent.
10. (Currently Amended) Use of Method of treating a cell proliferative disorder comprising
administering to a patient benefiting from such a treatment at least one M4-(N-substituted amino)-2-butynyl-1-esters M4-(N-substituted amino)-2-butynyl-1-ester represented by the following general formula I, their bis-(2-butynyl)diesters its bis-(2-butynyl)diester and/ or a pharmaceutically acceptable salts salt thereof,



wherein

R is a hydrogen atom; a straight-chained or branched, saturated or unsaturated aliphatic radical with 1-20 C-atoms which is unsubstituted or substituted one

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or more times by C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy, halogen, epoxy, amino, mercapto, a phenyl ring which is unsubstituted or substituted one or more times by C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy, epoxy, amino, mercapto or halogen; a cycloalkyl group with 4 to 7 atoms unsubstituted or substituted one or more times by C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy, epoxy, amino, mercapto or halogen,

R¹ and R² are joined to form a heterocyclic ring with 3 to 6 C-atoms, unsubstituted or substituted one or more times by C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy, halogen, epoxy, amino, mercapto, whereby at least one C-atom can be replaced by 0, S or N,

or

R¹ and R₂ R² are the same or different a hydrogen atom, a straight-chained or branched, saturated or unsaturated aliphatic radical with 1-20 C-atoms, unsubstituted or substituted one or more times by C₁-C₆-alkyl, C₁-C₆-alkoxy, hydroxy, halogen, epoxy, amino, mercapto,

in a cell proliferative disorder treating effective amount

~~for manufacturing an agent for the treatment of a cell proliferative disorder.~~

11. (Currently Amended) ~~Use according to claim 10,
characterized in that The method of claim 10, wherein~~
the cell proliferative disorder is a neoplasia.
12. (Currently Amended) ~~Use according to claim 10 or 11,
characterized in that,~~
~~the neoplasia The method of claim 11, wherein~~ the neoplasia is selected from the group consisting of leukemias, lymphomas, sarcomas, carcinomas, neural cell

- tumors, squamous cell carcinomas, germ cell tumors, undifferentiated tumors, seminomas, melanomas, neuroblastomas, mixed cell tumors, metastatic neoplasia and neoplasia due to pathogenic infections.
13. (New) 4-(N-substituted amino)-2-butynyl-1-esters according to claim 5, wherein R is methyl, ethyl, propyl, butyl, pentyl, hexyl, phenyl, tertiary butyl or cyclohexyl.
 14. (New) Pharmaceutical composition for use in therapy, comprising a compound according to claim 3, and a pharmaceutically-acceptable carrier, adjuvant, vehicle and/or diluent.
 15. (New) A kit for inhibiting abnormal cell growth comprising at least one of the esters of claim 1, bis-(2-butynyl) diesters or pharmaceutically acceptable salts thereof, and, in a separate container, information about using parts of the kit.